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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
EPPERSON, JON D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 10/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,621	HERPIN ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-29* is/are pending in the application.

4a) Of the above claim(s) *22-28* is/are withdrawn from consideration.

5)☒ Claim(s) *29* is/are allowed.

6)☒ Claim(s) *15-21* is/are rejected.

7)☒ Claim(s) *15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/11/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

Status of the Application

1. Receipt is acknowledged of a Response to a Restriction Requirement, which was dated on July 20, 2005.

Status of the Claims

2. Claims 15-29 are pending in the present application.

3. Applicant's response to the Restriction and/or Election of Species requirements is acknowledged (Applicant elected ***without traverse*** Group I, claims 15-21 and 29) and claims 22-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim (see below i.e., ***Response to Restriction and/or Election of Species***).

4. Please note: Applicant's elected species (N-butyl-1-(3,4-dichlorobenzoyl)-4-phenylsulfonylpiperazine-2-carboxamide) was searched and was not found in the prior art. Thus, the search was expanded to non-elected species, which *were* found in the prior art, see rejections below. See MPEP § 803.02 (emphasis added):

> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. ***The prior art search, however, will not be extended unnecessarily to cover all nonelected species***. Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that

anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

5. Therefore, claims 15-21 and 29 are examined on the merits in this action.

Response to Restriction and/or Election of Species

6. Applicant's election of Group I (claims 15-21 and 29) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a) and/ or 37 CFR 1.111(b)) (e.g., see 7/20/05 Response, pages 1-2 wherein Applicants took issue with the "characterization" of Group I, but did not indicate in any way that the restriction was improper).

7. Applicant's election of species is also acknowledged (i.e., see 7/20/05 Response, page 2). Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election of species has also been treated as an election without traverse (MPEP § 818.03(a) and/ or 37 CFR 1.111(b)).

8. As a result, the restriction requirement and/or election of species is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

9. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98 (b) requires a list of all patents, publications, or other information

submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on the form PTO-892, they have not been considered.

10. The references listed on applicant's PTO-1449 form have been considered by the Examiner. A copy of the form is attached to this Office Action (e.g., 6/11/02).

Specification

11. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Objections to the Claims

12. Claim 15 is objected to because of the following informalities:

A. Claim 15 contains two steps labeled "(5)", which appears to be a typographical error. Correction is requested.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 15-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Doll et al. (U.S. Patent No. 5,880,128) (Publication Date is **March 9, 1999**) and Sarantakis et al. (Sarantakis, D.; Bicksler, J. J. "Solid Phase Synthesis of Sec-Amides and Removal from the Polymeric Support Under Mild Conditions" *Tetrahedron Letters*. **1997**, *38(42)*, 7325-7328) and Greene et al. (Greene, T. H. and Wuts, P. G. M. Protective Groups in Organic Synthesis, 3rd edition, John Wiley & Sons, New York (**April 1999**)).

For ***claims 15, 18-21***, Doll et al. (see entire document) teach a process for preparing piperazinyl compounds (e.g., see Doll et al., "Process D for Preparing Piperazinyl Compounds" starting on column 27; see also Summary of Invention), which reads on Applicants' claimed method. For example, Doll et al. teach method steps for the preparation of compounds like 4-(diphenylacetyl)-N-methyl-1-(1-napthalenylsulfonyl)-2-piperazinecarboxyamide (e.g., columns 67, Entry 21; see also columns 27-30), which falls entirely within the scope of the diazacycloalkylcarboxy derivatives that are produced by Applicants' claimed method when the diazaheterocyclyl ring = six membered

piperazine ring, $L^1 = Y^1R^2$ and Y^1 = -C(O)- and R^2 = "aliphatic" $CHPh_2$, $L^2 = Y^2R^3$ and $Y^2 = -SO_2-$ and R^3 = aromatic naphthalene, and X = NHR^1 and $R^1 = -CH_3$. The $CHPh_2$ qualifies as an "aliphatic" group in this scenario because Applicants define said aliphatic group broadly in their specification (e.g., see page 7, lines 11-12, "Aliphatic means a radical derived from a non aromatic C-H bond by removal of the hydrogen atom. The aliphatic radical may be further substituted by ... aromatic radicals"). Doll et al. also teach method steps for the synthesis of said piperazinyl compounds on a solid support (e.g., see columns 27 and 28, Process D, step 1, wherein a "resin" is disclosed; see also columns 29 and 39), which reads on Applicants' step (1). In addition, Doll et al. disclose the use of a linker (e.g., see Process D, step 1, wherein "A-L-B" is disclosed), which reads on Applicants' step (2). Doll et al. also disclose (3) a process for removing one of P^1 or P^2 (e.g., see Process D, step 2, wherein either $-P^1$ or $-P^2$ are removed). Doll et al. also disclose (4) a process for introducing L^1 or L^2 (e.g., see Process D, step 3, wherein R^1Y^1 is introduced). Doll et al. also (5) disclose a process for the removal of the other P^1 or P^2 (e.g., see Process D, step 4, wherein a deprotection step for removing either P^1 or P^2 is disclosed). Doll et al. also disclose a process of introducing the other L^1 or L^2 (e.g., see Process D, step 5, wherein Y^2-(C=O)-Z is introduced), which reads on Applicants' "second" step (5) (e.g., see objection to claims above). Doll et al. also disclose a process for isolating the diazacycloalkylcarboxy derivative (e.g., see Process D, cleavage step; see also Examples wherein compounds are purified and isolated). Doll et al. also disclose protecting groups that can be removed by base- and/or metal-labile protecting groups including fmoc (i.e., 9-fluorenylmethoxycarbonyl), benzyl groups used Pd/C

hydrogenation (e.g., see column 29, 48-50; see also Examples). Furthermore, the use of nitrogen protecting groups such as Alloc and Fmoc were well known at the time of filing (e.g., see Greene et al., pages 503-507, 526 and 527) and, as a result, one of ordinary skill in the art would immediately envisage such steps (e.g., see *In re Graves*, 69 F.3d 1147, 36 USPQ2d 1697 (Fed. Cir. 1995); see also *In re Donohue*, 766 F.2d 531, 533 (Fed. Cir. 1985) (prior art anticipates or renders obvious a claim if it discloses the claimed invention such that a skilled artisan could take its teachings and his own knowledge to possess the claimed invention); see also *In re LeGrice*, 301 F.2d 929, 936 (C.C.P.A. 1962).

For ***claim 17***, Doll et al. disclose $-C_4N_2-$ (e.g., see Doll et al., column 1, lines 45-55 wherein X1 is N; see also lines 55-65; see also 4-(diphenylacetyl)-N-methyl-1-(1-napthalenylsulfonyl)-2-piperazinecarboxyamide species disclosed above).

The prior art teachings of Doll et al. differ from the claimed invention as follows:

For ***claims 15-16***, Doll et al. fail to teach the specific "alkylating" and "acylating" process steps shown in method steps (1) and (2). Doll et al. only state that the method for linking the piperidinyl compound to the resin in general terms (e.g., column 29, paragraph 1). However, Doll et al. do state that their claimed linkers can contain primary and/or secondary amines (e.g., see column 29, lines 22-23, "'-B' group ... primary or secondary amine").

However, Sarantakis et al. teach the following limitations that are deficient in Doll et al.:

For ***claim 15***, Sarantakis et al. (see entire document) teach method steps for linking molecules to a solid-support using one of Applicants' most preferred linkers (e.g.,

see Sarantakis et al., page 7326, scheme 1, compound 1 wherein (S)-CH_2-O-Ph(OCH_3)-CH=O is disclosed). The linker is used to make sec-amides (e.g., see Title) like the sec-amides disclosed by Doll et al. which involves both an "alkylation" step via reductive amination (e.g., see scheme 1, R_1NH_2 and $NaBH_4$/THF-EtOH method steps) and an "acylation" step via the use of an acid i.e., X = -OH (e.g., see scheme 1, R_2COX step leading to compound 4).

For ***claim 16***, Sarantakis et al. disclose (S)-CH_2-O-Ph(OCH_3)-CH=O (e.g., see page 7326, scheme 1, compound 1).

It would have been *prima facie* obvious to one skilled in the art at the time the invention was made to make the piperidinyl compounds as taught by Doll et al. with the linking method as disclosed by Sarantakis et al. because Sarantakis et al. explicitly state that their method is useful for making sec-amides (e.g., see Sarantakis et al., Title), which would encompass the sec-amides disclosed by Doll et al. (e.g., 4-(diphenylacetyl)-N-methyl-1-(1-napthalenylsulfonyl)-2-piperazinecarboxyamide, see above). Furthermore, one of ordinary skill in the art would have been motivated to use the linking method as taught by Sarantakis et al. because Sarantakis et al. explicitly state that sec-amides can be produced under "mild" conditions providing good yields with little side reactions (e.g., see Sarantakis et al., title; see also page 7325, paragraph 1; see also page 7327, paragraph 1, "The higher sensitivity of our sec-amide-resin bound to TFA in comparison to the primary-amides may be due to the increased basicity of the sec-amide bond which encourages easier protonation in the acidic deprotection medium"). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because

Sarantakis et al. teach that this is a general method that can be applied to for both peptidic and non-peptidic compounds and cite various references wherein reductive amination has been used in a variety of settings (see Sarantakis et al., page 7325, paragraph 1, references 3 and 4; see also page 7327, paragraph 1). In addition, a person of skill in the art would have been motivated to use the carbamate protecting groups as disclosed by Green et al. in the method disclosed by Doll et al. (e.g., Alloc and Fmoc) because Green et al. explicitly state the protecting groups reduce racemization and specially refer to the Alloc and Fmoc protecting groups as being the "most useful" and "readily cleavable" (e.g., see page 503, last paragraph). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because Greene et al. states that these protecting groups were "routinely" used in synthesis for a wide variety of reactions and provides many examples of such reactions (e.g., see Greene et al., pages 506, 507, 526 and 527).

Allowable Subject Matter

15. Claim 29 is allowed. The prior art does not teach or fairly suggest Applicants' claimed method for preparing the claimed substituted hydantoin with the formula shown in claim 29.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
October 12, 2005